

In the United States Court of Federal Claims

No. 15-734V

(E-Filed: April 30, 2019)¹

AMY N. HEDDENS,

Petitioner,

v.

SECRETARY OF HEALTH AND
HUMAN SERVICES,

Respondent.

)
) Vaccine (human papillomavirus);
) National Childhood Vaccine
) Injury Act of 1986, 42 U.S.C. §§
) 300aa-1 to -34 (2012); Deferential
) Review of the Special Master's
) Fact Finding and Weighing of the
) Evidence.
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Ronald C. Homer, Boston, MA, for petitioner.

Christine M. Becer, Trial Attorney, with whom were Joseph H. Hunt, Assistant Attorney General, C. Salvatore D'Alessio, Acting Director, Catharine E. Reeves, Deputy Director, Gabrielle M. Fielding, Assistant Director, Torts Branch, Civil Division, United States Department of Justice, Washington, DC, for respondent.

OPINION AND ORDER

CAMPBELL-SMITH, Judge.

On October 5, 2018, the special master issued his decision denying compensation in this vaccine case. See ECF No. 94. On October 31, 2018, petitioner filed: (1) a motion for review of the special master's decision, ECF No. 97; and (2) the memorandum in support of the motion for review, ECF No. 99. Respondent filed its response brief on

¹ Pursuant to Rule 18(b) of the Vaccine Rules of the United States Court of Federal Claims (Appendix B to the Rules of the United States Court of Federal Claims), this opinion was initially filed under seal on March 12, 2019. Pursuant to ¶ 4 of the ordering language, the parties were to propose redactions of the information contained therein on or before March 26, 2019. No proposed redactions were submitted to the court.

November 30, 2018. See ECF No. 102. Petitioner's motion is fully briefed and ripe for decision.

The special master denied petitioner compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 (2012) (the Vaccine Act). As explained below, the special master's entitlement decision survives this court's review. Accordingly, the court must **DENY** petitioner's motion for review.

I. Background

On June 30, 2010, petitioner visited a clinic for a "well woman exam." There, she reported "frequent urination, loss of balance, and blurry vision when she moved her head," as well as diarrhea, a late period, and nausea. ECF No. 94 at 2; see also ECF No. 96 at 19-21 (transcript of the evidentiary hearing held on October 1, 2018).

On December 3, 2012, petitioner received her third dose of the human papillomavirus (HPV) vaccine. ECF No. 94 at 2. On January 18, 2013, petitioner experienced "double vision and dizziness." Id. She went to an urgent care facility for evaluation. Id. The urgent care doctor referred petitioner to an emergency room, from which she was referred to an ophthalmologist. Id. On January 29, 2013, petitioner received a magnetic resonance imaging scan (MRI) that showed "multiple enhancing lesions" throughout her brain. Id. Thereafter, a neurologist diagnosed petitioner with multiple sclerosis (MS). Id. On July 16, 2015, petitioner requested Vaccine Act compensation on the theory that her MS "was caused-in-fact" by the HPV vaccine. ECF No. 1 (petition). In her memorandum in support of her motion for review, petitioner characterizes her claim as alleging "that her HPV vaccination caused a significant aggravation of an underlying, subclinical MS." ECF No. 99 at 6.

On October 1, 2018, the special master held an evidentiary hearing. See ECF No. 96. During the hearing, the special master heard testimony from both petitioner's expert, Dr. Salvatore Napoli, and respondent's expert, Dr. Subramaniam Sriram. See id. At the close of the hearing, the special master issued a ruling from the bench and denied petitioner's request for compensation. See id. at 229-53. In issuing his ruling, the special master explained: "[W]hat I look at first is the epidemiology, and that does not seem to support the theory that HPV vaccine causes or affects multiple sclerosis. I realize that [Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274 (Fed. Cir. 2005),] says that epidemiology is not required, but epidemiology remains a relevant factor." Id. at 239. He also stated:

I tend to give the epidemiology great weight. That's how I tend to view the evidence. I think [Whitecotton v. Sec'y of Health & Human Servs., 81 F.3d 1099 (Fed. Cir. 1996),] says that how much weight Special Masters give to evidence is a discretionary function of a Special Master. So I think some

Special Masters may weigh epidemiology different[ly] than I do, but I tend to give it more weight.

Id. at 242.

The bench ruling was later memorialized in a written decision issued four days later, on October 5, 2018. See ECF No. 94. As an initial matter, the special master explained that: “the undersigned considered all the evidence, including the medical records, expert reports, medical articles, and oral testimony.” Id. at 1-2. The special master reiterated his conclusion that petitioner had failed to carry her burden of demonstrating that “the HPV vaccine can worsen (or cause) MS,” and concluded that “regardless of whether her claim is one for significant aggravation . . . or whether her claim is a new onset claim, she is not entitled to compensation.” Id. at 6.

The special master’s decision noted that the “undisputed testimony from the experts indicate[s] the [petitioner], most likely, had lesions in her brain before the HPV vaccination on December 3, 2012.” Id. at 2-3. For this reason, the special master analyzed petitioner’s case “as a claim for significant aggravation,” and applied the factors set forth in this court’s opinion in Loving v. Sec’y of Health & Human Servs., 86 Fed. Cl. 135, 144 (2009). The special master noted that “[t]his decision turns on the outcome of the fourth Loving factor . . . whether the HPV vaccination can cause an exacerbation of MS.” Id.

From there, the special master proceeded to evaluate expert testimony, along with epidemiological and experimental evidence. The epidemiological evidence included a variety of studies that had been submitted by respondent in an effort to undermine petitioner’s claim—some, but not all of which, addressed the connection between the HPV vaccine and MS. See id.; see also id. at 3-4 (describing and citing to the studies presented by respondent). The special master assigned “less evidentiary value” to the studies that did not specifically involve the HPV vaccine. Id. at 4. He concluded that the studies did not tend to support petitioner’s case but also observed that “epidemiology does not conclusively establish that the HPV vaccine cannot cause MS.” Id. As such, the conclusion that petitioner failed to carry her burden under the fourth Loving factor “does not rest exclusively on the epidemiology.” Id.

Petitioner’s expert posited a theory that molecular mimicry explains the connection between the HPV vaccine and MS, and offered two articles as support. Id. at 4-5. The first article, by Kai W. Wucherpfennig and Jack L. Strominger,² “explored

² Kai W. Wucherpfennig & Jack L. Strominger, Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein, 80(5) Cell 695 (1995). See ECF No. 94 at 4 n.11.

whether various foreign antigens (viruses and bacteria) could inspire the production of T cells that would react with myelin basic protein.” Id. A review of relevant data revealed that “the human papillomavirus did not generate a strong response” in this context. Id. at 5. The second article, by Darja Kanduc,³ addressed the HPV vaccine, and proposed that cross-reactivity with certain proteins could cause complications. See id. “But, none of those problems resemble the problems that appear in MS.” Id. The special master acknowledged that these articles presented possible theories, but concluded that they were not persuasive enough to carry petitioner’s burden. Id. at 5-6.

II. Legal Standards

This court has jurisdiction to review the decision of a special master in a Vaccine Act case. 42 U.S.C. § 300aa-12(e)(2). “Under the Vaccine Act, the Court of Federal Claims reviews the decision of the special master to determine if it is ‘arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law[.]’” de Bazan v. Sec’y of Health & Human Servs., 539 F.3d 1347, 1350 (Fed. Cir. 2008) (quoting 42 U.S.C. § 300aa-12(e)(2)(B) and citing Althen, 418 F.3d at 1277) (alteration in original).

This court uses three distinct standards of review in Vaccine Act cases, depending upon which aspect of a special master’s judgment is under scrutiny.

These standards vary in application as well as degree of deference. Each standard applies to a different aspect of the judgment. Fact findings are reviewed . . . under the arbitrary and capricious standard; legal questions under the “not in accordance with law” standard; and discretionary rulings under the abuse of discretion standard.

Munn v. Sec’y of Dep’t of Health & Human Servs., 970 F.2d 863, 870 n.10 (Fed. Cir. 1992).

The third standard of review, abuse of discretion, is applicable when the special master excludes evidence or otherwise limits the record upon which he or she relies. See id. at 870. As this court has stated, the third standard applies to the special master’s evidentiary rulings. Stillwell v. Sec’y of Health & Human Servs., 118 Fed. Cl. 47, 55 (2014) (citation omitted), aff’d, 607 F. App’x 997 (Fed. Cir. 2015). Determinations subject to review for abuse of discretion must be sustained unless “manifestly erroneous.” Piscopo v. Sec’y of Health & Human Servs., 66 Fed. Cl. 49, 53 (2005) (citations omitted); see also Milmark Servs., Inc. v. United States, 731 F.2d 855, 860 (Fed. Cir. 1984) (holding that decisions within the trial court’s discretion are to be sustained unless “manifestly erroneous”) (citation omitted).

³ Darja Kanduc, Quantifying the possible cross-reactivity risk of an HPV16 vaccine, 8 J. Experimental Therapeutics & Oncology 65 (2009). See ECF No. 94 at 5 n.12.

A petitioner may obtain compensation if she “sustained, or had significantly aggravated, any illness, disability, injury, or condition not set forth in the Vaccine Injury Table but which was caused by” certain vaccines, including the HPV vaccine. 42 U.S.C. § 300aa-11(c)(1)(C)(ii). A case for significant aggravation of an off-Table claim requires proof, by a preponderance of the evidence of:

(1) the person’s condition prior to administration of the vaccine, (2) the person’s current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person’s current condition constitutes a “significant aggravation” of the person’s condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; see also W.C. v. Sec’y of Health & Human Servs., 704 F.3d 1352, 1360 (Fed. Cir. 2013) (referring to the Loving test as “the correct law”).

III. Analysis

In her memorandum in support of her motion for review, petitioner raises four objections to the special master’s decision. First, petitioner objects to the special master’s reliance on epidemiological studies that do not address the HPV vaccine. See ECF No. 99 at 15-16. Second, petitioner objects to the special master’s reliance on an article by Nikolai Madrid Scheller.⁴ Id. at 17-19. Third, petitioner objects more generally to the special master’s reliance on epidemiology. Id. at 19-25. And fourth, petitioner objects to the special master’s determination that she failed to meet her burden under Loving factor four by presenting a theory of molecular mimicry. Id. at 25-31. The court will address each argument in turn.

A. The Special Master Did Not Abuse His Discretion in Considering Studies that Did Not Involve the HPV Vaccine

Regarding her first objection, petitioner argues that the special master “gave substantial weight to epidemiologic studies that did not examine the HPV vaccination and MS.” ECF No. 99 at 15. Petitioner asserts that the special master’s “reliance on these studies in any capacity is not in accordance with the law.” Id. at 16. In particular, petitioner argues that such consideration violates the standard observed in Moberly v.

⁴ Nikolai Madrid Scheller et al., Quadrivalent HPV Vaccination and Risk of Multiple Sclerosis and Other Demyelinating Diseases of the Central Nervous System, 313 J. Amer. Med. Ass’n 54 (2015). See ECF No. 94 at 3 n.6.

Secretary of Health & Human Services, 592 F.3d 1315 (Fed. Cir. 2010), that “[a]s a general matter, epidemiological studies are designed to reveal statistical trends only for a carefully constructed test group. Such studies provide no evidence pertinent to persons not within the parameters of the test group.” Id. (quoting Moberly, 592 F.3d at 1324).

Petitioner is correct that some of the studies cited by the special master do not involve the HPV vaccine.⁵ The special master, however, acknowledged as much, and weighted the evidence accordingly. See ECF No. 94 at 4. He stated: “Because these studies are not about the HPV vaccine, they carry less evidentiary value than the epidemiology directly on point. But, to the extent these additional studies contribute to the analysis, they tend to show that vaccinations do not contribute to MS.” Id. In vaccine cases, a special master “must consider all relevant and reliable evidence governed by principles of fundamental fairness to both parties.” Rule 8(b)(1) of the Vaccine Rules of the United States Court of Federal Claims, Appendix B to the Rules of the United States Court of Federal Claims. And as the United States Court of Appeals for the Federal Circuit has held, “epidemiological studies are probative medical evidence relevant to causation.” Grant v. Sec’y of Dep’t of Health & Human Servs., 956 F.2d 1144, 1149 (Fed. Cir. 1992). See also Andreu ex rel. Andreu v. Sec’y of Dep’t of Health & Human Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009) (stating that although a “claimant need not produce medical literature of epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury”).

Neither party has cited, nor is the court aware of, any precedent requiring a special master to wholly reject consideration of epidemiological evidence if such evidence is not directly applicable to the facts of the case at bar. See, e.g., D’Tiole v. Sec’y of Health & Human Servs., 726 F. App’x 809, 811 (Fed. Cir. 2018) (“Nothing in Althen or [Capizzano v. Sec’y of Health & Human Servs., 440 F.3d 1317 (Fed. Cir. 2006)] requires the Special Master to ignore probative epidemiological evidence that undermines petitioner’s theory.”); Grant, 956 F.2d at 1148-49 (considering negative epidemiological evidence). Moreover, the special master explicitly stated that the “epidemiology does not conclusively establish that the HPV vaccine cannot cause MS.” ECF No. 94 at 4. For this reason, his conclusion “does not rest exclusively on the epidemiology.” Id.

It is clear to the court that the special master considered the epidemiological evidence presented by respondent, but did not treat that evidence as weighing heavily

⁵ The articles included in this section of the special master’s decision are: Frank DeStefano et al., Vaccinations and Risk of Central Nervous System Demyelinating Diseases in Adults, 60 Arch. Neurol. 504 (2003) and Christian Confavreux et al., Vaccinations and the Risk of Relapse in Multiple Sclerosis, 344 N. Eng. J. Medicine 319 (2001). See ECF No. 94 at 4 nn.8-9.

against petitioner, much less determinative of the issue at bar. The court, therefore, cannot agree that the special master abused his discretion by citing to the studies that respondent submitted in reaching his decision.

B. The Special Master Did Not Abuse His Discretion by Failing to Address Every Flaw in the Scheller Study

In her second objection, petitioner alleges that the special master failed to account for various flaws in the Scheller study—another study offered into evidence by respondent. ECF No. 99 at 19. “[P]etitioner agrees that the overall conclusion of the Scheller study did not find a statistically significant increased risk of demyelinating disease following the HPV vaccination,” *id.* at 17, but claims that the special master’s “heavy reliance on the Scheller study, without acknowledgment of the flaws of the study, concessions of respondent’s expert, and importantly, a showing of higher crude incidence rate of MS in the vaccinated population aged 30-44, constitutes an abuse of discretion,” *id.* at 19.

The special master cited the Scheller study as one of several epidemiological studies in his written decision, before stating that “[c]ollectively, these studies did not support [petitioner’s] argument that the HPV vaccine can aggravate (or cause) MS.” ECF No. 94 at 3-4. Put another way, the special master concluded that the studies presented by respondent did not support petitioner’s case. Nor does petitioner claim that had the special master accounted for the flaws she alleges, the study would have assisted her in carrying the burden of proof. And in any event, as the court noted with respect to petitioner’s first objection, the special master explicitly stated that his conclusion “does not rest exclusively on the epidemiology.” ECF No. 94 at 4.

Moreover, as instructed by the Federal Circuit, the court “generally presume[s] that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.” Moriarty v. Sec’y of Health & Human Servs., 844 F.3d 1322, 1328 (Fed. Cir. 2016). See also ECF No. 96 at 232 (the special master stating “I think I have considered all of the evidence even though I may not mention everything”). Petitioner’s own brief outlines the testimony elicited at the evidentiary hearing from respondent’s expert addressing a number of the alleged weaknesses in the Scheller study. See ECF No. 99 at 17-18. As such, the court will not presume—as petitioner asserts—that the special master failed to consider various ways in which the Scheller study may not directly apply to petitioner’s case.

For these reasons, it was not an abuse of discretion to cite the Scheller study without also reciting all of petitioner’s objections to that study.

C. The Special Master Did Not Abuse His Discretion in Considering Epidemiology and Did Not Elevate Petitioner's Burden of Proof

Petitioner's third objection is that the special master erred in placing "great weight" on epidemiology in his analysis, which allegedly had the effect of elevating petitioner's burden. ECF No. 99 at 24 ("To value epidemiology with such fervor, and specifically state that it is given 'great weight' compared to other special masters is an abuse of discretion, and not in accordance with law."); *id.* at 25 (arguing that "[t]he weight with which the Special Master relied on epidemiology is an abuse of discretion, which heightened petitioner's burden").

As the court has noted several times in the course of this short opinion, the special master explicitly stated that the "epidemiology does not conclusively establish that the HPV vaccine cannot cause MS," and for this reason, his conclusion "does not rest exclusively on the epidemiology." ECF No. 94 at 4. The special master also acknowledged from the bench that "there's a limit to epidemiology," that petitioner "is not required to submit epidemiology to prove [her] case," and that "epidemiology cannot prove a negative no matter how large the study." ECF No. 96 at 242-43. And because the special master "consider[ed] the record as a whole," the decision did not rest entirely—or even primarily—on his view of the epidemiology. *Id.* at 231.

There is simply no indication in the special master's decision that he regarded the epidemiological evidence with what petitioner calls "fervor," even if he expressed a preference, that may or may not differ from other special masters, for considering such evidence.

And as to petitioner's claim that the weight given to epidemiological studies had the effect of heightening petitioner's burden, the court does not agree. Petitioner's brief does not explain this contention in any detail. The court understands it, however, to be an argument that because the special master allegedly over-valued epidemiological evidence submitted by respondent, that consideration became an additional obstacle to petitioner proving her case. The special master, however, did not inappropriately value the epidemiological evidence submitted by respondent. And he did not conclude that the evidence disproved—or even weighed against—petitioner's theory. He simply stated that "[c]ollectively, these studies did not support [petitioner's] argument that the HPV vaccine can aggravate (or cause) MS." ECF No. 94 at 4. The court fails to see how this impacts, much less heightens, petitioner's burden.

D. The Special Master Did Not Abuse His Discretion in Analyzing Petitioner's Proof of Causation

Petitioner's fourth objection challenges the special master's ruling on Loving factor four. Petitioner's position is that molecular mimicry between the HPV vaccine and

myelin basic protein “activates T cells that are cross-reactive with self-antigens,” thereby triggering an immune reaction. ECF No. 99 at 26. The special master determined that the molecular mimicry theory was insufficient to carry petitioner’s burden, because she did not present persuasive empirical evidence to support the notion that the HPV vaccine can aggravate MS. See ECF No. 94 at 4.

To satisfy Loving factor four, a petitioner “must provide a reputable medical or scientific explanation that pertains specifically to the petitioner’s case, although the explanation need only be ‘legally probable, not medically or scientifically certain.’” Moberly, 592 F.3d at 1322 (quoting Knudsen v. Sec’y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)). For a theory to be “probable,” it must be more than merely “plausible” or “possible.” Id.; see also LaLonde v. Sec’y of Health & Human Servs., 746 F.3d 1334, 1339 (Fed. Cir. 2014) (“simply identifying a ‘plausible’ theory of causation is insufficient for a petitioner to meet her burden of proof”) (citing Moberly, 592 F.3d at 1322).

Petitioner challenges the way the special master analyzed petitioner’s molecular mimicry theory. The special master discounted the Wucherpfennig article because, in his view, that study did not find that HPV produced a “strong response” in terms of T-cell count. ECF No. 94 at 5; see also ECF No. 96 at 156 (respondent’s expert indicating that “the HPV sequences [did not] stimulate the T cell clones”). Petitioner does not seriously contest that finding. Instead, petitioner focuses on the special master’s treatment of the Kanduc article. ECF No. 99 at 27-28.

The special master discounted the Kanduc article. In his view, the “various problems” identified by Kanduc as resulting from cross-reactivity do not “resemble the problems that appear in MS.” ECF No. 94 at 5. According to petitioner, Kanduc described “82 perfect overlaps between HPV16 and the human proteome, any of which could trigger autoimmunity in a predisposed individual.” ECF No. 99 at 28. The special master treated these overlaps as “possible” scenarios for cross-reactivity, but not as a “reliable basis for elevating this potentiality to a probability.” ECF No. 94 at 5.

Before reaching this conclusion, the special master heard testimony on petitioner’s theory from her expert during the evidentiary hearing. See ECF No. 96 at 57-60 (discussing molecular mimicry in the context of MS and discussing the Wucherpfennig and Kanduc articles). Petitioner’s expert testified at several points during the hearing that the HPV vaccine has the potential to trigger MS. See, e.g., id. at 97 (stating that the HPV vaccine “can potentially” trigger MS, but also stating that he advises his MS patients to get vaccines); id. at 99 (noting, with regard to the Wucherpfennig article, that “one of the things that I kind of garner from the article is that there is the potential that activated T cell clones can autoreact against proteins on HPV”); id. at 99-100 (“[O]ne of the important points I thought about . . . Wucherpfennig is that it may not have the most robust response, . . . but there is the potential that it could.”); id. at 129 (acknowledging

that the Kanduc article does not state “that the HP[V] vaccine can cause MS”); id. at 131-32 (petitioner’s expert stating that he has not “been able to provide any studies that demonstrate a causal relationship between the HPV vaccine and MS,” but has offered studies that “it can create an autoimmune response”).

After explaining at considerable length the framework of his analysis, the special master concluded that petitioner’s evidence of an exacerbated injury due to molecular mimicry was insufficient. In reference to petitioner’s expert’s testimony, the special master explained at the October 1, 2018 evidentiary hearing, as follows:

[O]n some level you can’t say that to say there is potential reaction is erroneous because you could always say there is a potential for a reaction, but . . . I think the . . . potentiality is not the same thing as meeting a preponderance of the evidence.

Id. at 245. In his written decision, the special master held that petitioner “has provided no reliable basis for elevating the potentiality [of molecular mimicry] to a probability.” ECF No. 94 at 5.

In the court’s view, the special master did not err in his consideration of the molecular mimicry theory. Petitioner’s objection to his analysis is more a disagreement with his exercise of discretion than the identification of legal error. Petitioner argues that the special master “discount[ed] the evidence supporting her theory and, instead, require[d] direct proof of petitioner’s proffered mechanism.” ECF No. 99 at 30. The record does not support this position. The special master conducted a lengthy colloquy with petitioner’s expert, reviewed the articles petitioner’s expert presented on the subject, and specifically stated that he considered all of the evidence presented before reaching his decision. The court cannot accept petitioner’s invitation to reweigh the evidence. See Porter v. Sec’y of Health & Human Servs., 663 F.3d 1242, 1249 (Fed. Cir. 2011) (stating that the reviewing court does not “reweigh the factual evidence, assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses—these are all matters within the purview of the fact finder”) (citations omitted).

For these reasons, petitioner’s motion for review must be denied, and the special master’s decision denying compensation must be affirmed.

IV. Conclusion

For the above-stated reasons, the court sustains the entitlement decision of the special master. Accordingly, it is hereby **ORDERED** that:

- (1) Petitioner’s motion for review, ECF No. 97, is **DENIED**;

- (2) The decision of the special master, filed October 5, 2018, is **SUSTAINED**;
- (3) The clerk's office is directed to **ENTER** final judgment in accordance with the special master's decision of October 5, 2018; and
- (4) The parties shall separately **FILE** any proposed redactions to this opinion, with the text to be redacted clearly blacked out, on or before **March 26, 2019**.

IT IS SO ORDERED.

s/Patricia E. Campbell-Smith
PATRICIA E. CAMPBELL-SMITH
Judge